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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/783,620

02/20/2004

Liwen Jiang

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EXAMINER

KUMAR, VINOD

ART UNIT

PAPER NUMBER

1638

MAIL DATE

DELIVERY MODE

04/22/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/783,620	<b>Applicant(s)</b> JIANG ET AL.	
	<b>Examiner</b> VINOD KUMAR	<b>Art Unit</b> 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 22 January 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,7-9,13,15 and 17-29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,7-9,13,15 and 17-29 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02/20/2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Status of Objections and Rejections***

1. Amendment filed in the paper of January 22, 2008 is entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 7-9, 13, 15, and 17-29 are pending.

Claims 1, 7-9, 13, 15, and 17-29 are examined on merits in this Office action.

### ***Election/Restrictions***

2. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### ***Claim Rejections - 35 USC § 112***

3. Claims 1, 7-9, 13, 15, and 17-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in its recitation "wherein at least a part of the target proteins is separated from the

anchors” in line 8, which is confusing since it unclear which part of the target proteins is separated from which anchors. It is unclear what is intended?

Dependent claims 7-9, 13, 15, and 17-29 are also rejected because they fail to overcome the deficiency of claim 1.

This rejection has been necessitated due to the claim amendment filed in the paper of January 22, 2008.

4. Claims 1, 7-9, 13, 15, and 17-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 recites “wherein at least a part of the target proteins is separated from the anchors” in line 8 which introduces **NEW MATTER** into amended claim. The specification does not provide written description support for "at least a part of the target proteins is separated from the anchors". This does not comply with written description requirements.

Dependent claims 7-9, 13, 15, and 17-29 are also rejected because they fail to overcome the deficiency of claim 1.

This rejection has been necessitated due to the claim amendment filed in the paper of January 22, 2008.

Applicant's response filed in the paper of January 22, 2008 refers to figures 4-8, example 4, and paragraphs 53-54 of the specification for the support of the phrase "

wherein at least a part of the target proteins is separated from the anchors” (response, page 6, lines 7-10). However, it is noted that cited figures and pages of the specification do not support the phrase “wherein at least a part of the target proteins is separated from the anchors”.

***Claim Rejections - 35 USC § 103***

5. Claims 1, 7-9, 13, 15, and 17-29 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Jiang et al. (The Journal of Cell Biology, 143:1183-1199, 1998) in view of Zheng et al. (Plant Physiol., 109:777-786, 1995) and Goddijn et al. (Trends Biotechnol. 13: 379-387, 1995) for the reasons of record stated in the Office action September 20, 2008.

It is maintained that Jiang et al. teach a DNA construct comprising a promoter sequence (35S CaMV) operably linked with a first DNA sequence encoding proaleurain (target protein), wherein the first DNA sequence is further operably linked with a second DNA sequence encoding a transmembrane domain (TMD) of a BP-80 or  $\alpha$ -TIP protein and a cytoplasmic tail (CT) sequence of a BP-80 or  $\alpha$ -TIP protein, and which serve as anchors for delivering the target protein to sub-compartments of protein storage vacuoles of the plant cells. The reference also teaches that  $\alpha$ -TIP CT prevents traffic of the target protein through the Golgi and causes it to be localized in organelles separated from ER and from Golgi and LV prevacuolar compartment markers (see in particular, pg 1183, abstract, line bridging left and right columns of abstract).

The reference further teaches that the second nucleic acid sequence is further operably linked with a third nucleic acid sequence that functions as transcription termination region (NOS terminator in pBI221 vector). The reference further teaches that the construct comprises a spacer sequence operably linked to 5' end of TMD. The spacer sequence taught in the reference encodes an amino acid sequence which has 100% sequence identity to instant SEQ ID NO: 8.

The reference further teaches that sub-compartments comprise globoids and crystalloids. The reference further teaches a proteolytic cleavage sequence Kex2 between 3' end of the target protein sequence and 5' end of TMD. The reference also teaches association of protease activity within protein storage vacuole that acts on the proteolytic cleavage sequence so that target protein separates from the transmembrane domain. The reference further teaches proaleurain signal peptide sequence present at the 5' end of target sequence (proaleurain). The DNA construct taught in the reference was used to transform tobacco suspension culture protoplasts. See in particular, page 1183, abstract; page 1184, column 2<sup>nd</sup> through the end of first paragraph of column 1<sup>st</sup> of page 1185; page 1186, results, figure 1; page 1187, table 1; page 1188, figure 2; page 1189, figures 3 and 4; page 1190, figure 5; page 1191, table II, figure 6; page 1192, figure 7; page 1194, table III; page 1196, figure 10.

Jiang et al. do not teach a seed specific promoter.

Zheng et al. teach glutelin Gt1 gene promoter which is a seed-specific promoter. The reference further teaches that said promoter directed the expression of phaseolin (target gene of interest) in a seed-specific manner. The transgenic seed storage protein

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phaseolin accumulated up to 4% in vacuolar protein bodies of transgenic rice seeds.

The reference also teaches that seed-specific promoter, such as, glutelin Gt1 gene promoter can be used in obtaining high and stable expression of a foreign protein of interest in the transgenic seeds. See in particular, page 777, abstract; page 778, materials and methods; page 780, figures 1 and 3; page 781, figures 4 and 5; page 782, figures 6 and 7; page 783 figure 8; page 784, figure 9.

Goddijn et al. (Trends Biotechnol. 13: 379-387, 1995) teach that it is well known in the art that seeds can also be used as "bioreactors" for the production of pharmaceutically or industrially important products. See the entire article.

It is, therefore, maintained that It would have been prima facie obvious and within the scope of an ordinary skill in the art at the time the claimed invention was made to modify Jiang et al. DNA construct by operably linking a target coding sequence encoding a protein of interest to any seed-specific promoter including Zheng et al. seed-specific promoter for the purpose of obtaining high levels of seed-specific expression of the target protein in the transgenic seeds tissues. It would have been obvious and within the scope of an ordinary skill in the art to use any method of plant transformation, including *Agrobacterium tumefaciens* Ti plasmid mediated method of plant transformation as taught by Zheng et al. to obtain transgenic seeds overexpressing high levels of transgenic protein of interest with reasonable expectation of success.

It is further maintained that given Goddijn et al. teach that seeds can be used as "bioreactors" for the production of pharmaceutically or industrially important products, and Zheng et al. teach that a seed-specific promoter (e.g. glutelin Gt1 gene promoter)

has the property of directing stable and high levels of seed-specific expression of a transgenic protein of interest, one of the ordinary skill in the art would have been motivated to overexpress said transgenic protein of interest specifically in seeds to arrive at the claimed invention with reasonable expectation of success.

Applicant traverses the rejection in the paper filed on January 22, 2008.

Applicant argues that Jiang et al. reference does not disclose or suggest a result in the tobacco cells transfected with the construct comprising the alpha-Tip CT that indicates target proteins separated from the anchors and found in the cell soluble (CS) fraction. Applicant further argues that Jiang et al. do not teach or suggest that the target proteins should be separated from the anchors in the real protein storage vacuoles (PSVs) of tobacco cells, much less PSVs of tobacco seeds, and release to the CS component. Applicant further argues that Jiang et al. do not cover the technical features recited in claim 1, and there is no teaching that Jiang et al. reference that proteins expressed in tobacco seeds with a seed specific promoter can be directed by the alpha-Tip CT sequence bypassing the Golgi into a PSV crystalloid (response, page 6, lines 18-23; line 24 through the end of 1<sup>st</sup> paragraph of page 24).

Applicant's arguments were fully considered but were deemed to be unpersuasive.

It is maintained that Jiang et al. clearly teach that protein of interest would be directed to the PSV crystalloid via a direct ER-PSV pathway, and thus bypassing Golgi of cells (see abstract). It is further maintained that by combining the teachings of Jiang et al. and Zheng et al., one of ordinary skill in the art would have arrived at the instantly claimed construct, which would have directed the target protein of interest to the PSV



crystalloid via a direct ER-PSV pathway with reasonable expectation of success. It is important to note that the modified construct of Jiang et al. would have produced the expected results because it is structurally and functionally identical to the instantly claimed construct.

Applicant is reminded that the features upon which applicant relies (i.e. target protein is found in CS fraction) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). It would have been obvious and within the scope of an ordinary skill in the art to expect that target proteins would have separated from anchors because anchors would have delivered the target protein to sub-compartments of protein storage vacuoles with reasonable expectation of success.

It is also important to note that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In the instant case, Jiang et al. teach all the structural elements required to practice the invention, except for a seed-specific promoter. Zheng et al. provides motivation for incorporating a seed-specific promoter in Jiang et al. construct to obtain high levels and stable accumulation of foreign protein of interest in vacuolar protein bodies, and Goddijn et al. clearly teach the importance of

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using seeds as bioreactors in expressing a protein of interest. Thus it would have been obvious and within the scope of an ordinary skill in the art to have combined prior art teachings of Jiang et al., Goddijn et al. and Zheng et al. to arrive at the instantly claimed invention with reasonable expectation of success.

Thus it is maintained that the claimed invention as a whole is prima facie obvious over the combined teachings of the prior art.

### ***Conclusions***

6. Claims 1, 7-9, 13, 15, and 17-29 remain rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is set to expire within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Contact Information***


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vinod Kumar whose telephone number is (571) 272-4445. The examiner can normally be reached on 8.30 a.m. to 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong T. Bui/

Primary Examiner, Art Unit 1638

<div><div><div>Application Number</div><div></div></div></div>	Application/Control No.	Applicant(s)/Patent under Reexamination	
	10/783,620	JIANG ET AL.	
	Examiner	Art Unit	
	VINOD KUMAR	1638	